

AMENDMENT

In the Claims

The following Listing of Claims, in which deleted text appears as ~~struck through~~ and inserted text appears underlined, will replace all prior listings, and versions, of claims in the application.

Listing of Claims

Claim 1 (cancelled)

Claim 2 (previously presented): The method of claim 68, wherein said subject is a human.

Claim 3 (previously presented): The method of claim 2, wherein said one or more interferons formulated for short-term delivery are selected from the group consisting of natural ~~or~~ and recombinant alpha, beta, consensus, gamma, leukocyte, omega, and tau interferon and versions thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety is attached.

Claim 4 (previously presented): The method of claim 3, wherein said interferon-responsive disorder is selected from the group consisting of viral hepatitis C, viral hepatitis B, condyloma accuminata, hairy cell leukemia, malignant melanoma, follicular lymphoma, AIDS-related Kaposi's sarcoma, multiple sclerosis, chronic granulomatous disease, pulmonary fibrosis, and tuberculosis.

Claim 5 (previously presented): The method of claim 3, wherein said interferon-responsive disorder is selected from the group consisting of viral hepatitis C, viral hepatitis B, condyloma accuminata, hairy cell leukemia, malignant melanoma, follicular lymphoma, and AIDS-related Kaposi's sarcoma; and said one or more interferons formulated for short-term delivery are selected from the group consisting of natural and recombinant alpha, consensus, leukocyte, omega and tau interferon and versions thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety is attached.

Claim 6 (previously presented): The method of claim 3, wherein said interferon-responsive disorder is selected from the group consisting of chronic granulomatous disease, pulmonary fibrosis, and tuberculosis; and said one or more interferons formulated for short-term delivery are selected from the group consisting of natural and recombinant gamma interferon and a version thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety is attached.

Claim 7 (previously presented): The method of claim 3, wherein said interferon-responsive disorder is multiple sclerosis; and said one or more interferons formulated for short-term delivery are selected from the group consisting of natural or recombinant alpha, beta, consensus, leukocyte, omega and tau interferon and versions thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety is attached.

Claim 8 (previously presented): The method of claim 3, wherein said one or more interferons formulated for short-term delivery are the same or different as said one or more interferons formulated for long-term delivery.

Claim 9 (previously presented): The method of claim 2, wherein said one or more interferons formulated for short-term delivery and said one or more interferons formulated for long-term delivery are independently selected from the group consisting of natural or recombinant alpha, beta, consensus, leukocyte, omega and tau interferon and versions thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety is attached.

Claim 10 (previously presented): The method of claim 2, wherein the short-term formulation and the long-term formulation are the same.

Claim 11 (previously presented): The method of claim 2, wherein the short-term formulation and the long-term formulation are different.

Claim 12 (previously presented): The method of claim 2, wherein said one or more interferons formulated for short-term delivery is a plurality of interferons and each short-term formulation is the same or different.

Claim 13 (previously presented): The method of claim 2, wherein said one or more interferons formulated for long-term delivery is a plurality of interferons and each long-term formulation is the same or different.

Claim 14 (previously presented): The method of claim 2, in which there is an overlap in the administration of the short-term formulation and the long-term formulation.

Claim 15 (previously presented): The method of claim 2, wherein the rates of short-term and long term delivery are substantially equivalent.

Claim 16 (previously presented): The method of claim 2, wherein the rates of short-term delivery and long term delivery are not substantially equivalent.

Claim 17 (previously presented): The method of claim 2, wherein the short-term formulation is delivered by injection, infusion, implant, transdermally, orally, parenterally, or by inhalational.

Claim 18 (cancelled)

Claim 19 (previously presented): The method of claim 13, wherein said one or more interferons formulated for long-term delivery are selected from the group consisting of natural and recombinant alpha, beta, consensus, gamma, leukocyte, omega, and tau interferon, and versions thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety is attached.

Claim 20 (previously presented): The method of claim 19, wherein said one or more interferons formulated for long-term delivery are selected from the group consisting of natural and recombinant omega interferon and versions thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety is covalently or non-covalently attached.

Claim 21 (cancelled)

Claim 22 (previously presented): The method of claim 74, wherein said individual subject is a human.

Claim 23 (cancelled)

Claim 24 (previously presented): The method of claim 22, wherein said interferon-responsive disorder is selected from the group consisting of viral hepatitis C, viral hepatitis B, viral hepatitis D, condyloma accuminata, hairy cell leukemia, malignant melanoma, multiple myeloma, follicular lymphoma, non-Hodgkin's lymphoma, cutaneous T-cell lymphoma, chronic myelogenous leukemia, basal cell carcinoma, mycosis fungoides, carcinoid syndrome, superficial bladder cancer, renal cell cancer,

colorectal cancer, laryngeal papillomatosis, actinic keratosis, Kaposi's sarcoma, multiple sclerosis, chronic granulomatous disease, pulmonary fibrosis, and tuberculosis.

Claim 25 (previously presented): The method of claim 22, wherein said interferon-responsive disorder is selected from the group consisting of viral hepatitis C, viral hepatitis B, viral hepatitis D, condyloma accuminata, hairy cell leukemia, malignant melanoma, multiple myeloma, follicular lymphoma, non-Hodgkin's lymphoma, cutaneous T-cell lymphoma, chronic myelogenous leukemia, basal cell carcinoma, mycosis fungoides, carcinoid syndrome, superficial bladder cancer, renal cell cancer, colorectal cancer, laryngeal papillomatosis, actinic keratosis, Kaposi's sarcoma; and said at least one interferon is selected from the group consisting of natural and recombinant alpha, consensus, leukocyte, omega and tau interferon and versions thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety is covalently or non-covalently attached.

Claim 26 (previously presented): The method of claim 22, wherein said interferon-responsive disorder is selected from the group consisting of chronic granulomatous disease, pulmonary fibrosis, and tuberculosis; and said at least one interferon is selected from the group consisting of natural and recombinant gamma interferon and a version thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety is covalently or non-covalently attached.

Claim 27 (previously presented): The method of claim 22, wherein said interferon-responsive disorder is selected from the group consisting of multiple sclerosis; and said at least one interferon is selected from the group consisting of natural and recombinant alpha, beta, consensus, leukocyte, omega and tau interferon and versions thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety is covalently or non-covalently attached.

Claim 28 (cancelled)

Claim 29 (previously presented): The method of claim 22, wherein said at least one interferon formulated for short-term delivery and said at least one interferon formulated for long-term delivery are independently selected from the group consisting of natural and recombinant alpha, beta, consensus, leukocyte, omega and tau interferon and versions thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety is covalently or non-covalently attached, and mixtures thereof.

Claim 30 (previously presented): The method of claim 22, wherein the short-term formulation and the long-term formulation are the same.

Claim 31 (previously presented): The method of claim 22, wherein the short-term formulation and the long-term formulation are different.

Claim 32 (previously presented): The method of claim 22, wherein said at least one interferon formulated for short-term delivery is a plurality of interferons and each short-term formulation is the same or different.

Claim 33 (previously presented): The method of claim 22, wherein said at least one interferon formulated for long-term delivery is a plurality of interferons and each long-term formulation is the same or is different.

Claim 34 (cancelled)

Claim 35 (previously presented): The method of claim 22, wherein the rates of short-term and long-term delivery are substantially equivalent.

Claim 36 (previously presented): The method of claim 22, wherein the rates of short-term delivery and long term delivery are not substantially equivalent.

Claim 37 (previously presented): The method of claim 23, wherein the short-term formulation is delivered by injection, infusion, implant, transdermally, orally, parenterally, or by inhalation.

Claim 38 (previously presented): The method of claim 37, wherein said at least one interferon formulated for short-term delivery is selected from the group consisting of natural and recombinant alpha, beta, consensus, gamma, leukocyte, omega, and tau interferon, and versions thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety is attached and mixtures thereof.

Claim 39 (cancelled)

Claim 40 (previously presented): The method of claim 33 wherein said at least one interferon formulated for long-term delivery is selected from the group consisting of natural and recombinant alpha,

beta, consensus, gamma, leukocyte, omega, and tau interferon, and versions thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety is attached and mixtures thereof.

Claim 41 (previously presented): A method of making a long-term drug delivery device, comprising:

a) determining a therapeutic and tolerable pharmacokinetic profile for a drug therapy in a subject by administering one or more drugs formulated for short-term delivery to said subject and monitoring said subject for therapeutic and adverse effects;

b) preparing an internally presentable, not externally programmable pump containing said one or more drugs formulated for long-term delivery in which said drugs are released from said pump at a first dosage rate; and

c) preparing a second internally presentable, not externally programmable pump for long-term delivery in which said one or more drugs are released at a fraction of said first dosage rate,

wherein each pump, alone or in combination, substantially achieves said pharmacokinetic profile during said long-term delivery.

Claim 42 (previously presented): The method of claim 41, wherein the fractional dosage rate is about fifty percent of said first dosage rate.

Claim 43 (previously presented): The method of claim 41, further comprising:

d) preparing dosing instructions for adjusting the rate of administration of said one or more drugs formulated for long-term delivery by employing one or a combination of the first or fractional dosage rate pumps.

Claim 44 (previously presented): The method of claim 41, wherein said one or more drugs is one or more interferons.

Claim 45 (previously presented): The method of claim 44, wherein said one or more interferons are selected from the group consisting of natural and recombinant alpha, beta, consensus interferon, gamma, leukocyte, omega, and tau interferon, and versions thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety is attached.

Claim 46 (previously presented): The method of claim 41, in which said one or more drugs are suitable for treating an interferon-responsive disorder.

Claim 47 (previously presented): The method of claim 46, wherein said interferon-responsive disorder is selected from the group consisting of viral hepatitis C, viral hepatitis B, viral hepatitis D, condyloma accuminata, hairy cell leukemia, malignant melanoma, multiple myeloma, follicular lymphoma, non-Hodgkin's lymphoma, cutaneous T-cell lymphoma, chronic myelogenous leukemia, basal cell carcinoma, mycosis fungoides, carcinoid syndrome, superficial bladder cancer, renal cell cancer, colorectal cancer, laryngeal papillomatosis, actinic keratosis, Kaposi's sarcoma, multiple sclerosis, chronic granulomatous disease, pulmonary fibrosis, and tuberculosis.

Claim 48 (cancelled)

Claim 49 (previously presented): The method of claim 46, wherein said interferon-responsive disorder is hepatitis C; and said one or more drugs is omega interferon.

Claim 50 (currently amended): The method of claim 46 wherein said interferon-responsive disorder is hepatitis C and ~~and~~ said one or more drugs is an alpha interferon.

Claim 51 (currently amended): The method of claim 46 wherein said interferon-responsive disorder is hepatitis C and ~~and~~ said one or more drugs is a consensus interferon.

Claim 52 (currently amended): The method of claim 46 wherein said interferon-responsive disorder is hepatitis C and ~~and~~ said one or more drugs is a natural or recombinant interferon.

Claim 53 (previously presented): The method of claim 46, wherein said interferon-responsive disorder is selected from the group consisting of chronic granulomatous disease, pulmonary fibrosis, and tuberculosis; and said one or more drugs is one or more interferons selected from the group consisting of natural and recombinant gamma interferon and a version thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety is attached and mixtures thereof.

Claim 54 (previously presented): The method of claim 44, wherein said interferon-responsive disorder is selected from the group consisting of multiple sclerosis; and said one or more drugs is one or more interferons selected from the group consisting of natural and recombinant alpha, beta, consensus,

leukocyte, omega and tau interferon and versions thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety is attached.

Claims 55-67 (cancelled)

Claim 68 (previously presented): A method of treating an interferon-responsive disorder in a subject, comprising:

a) determining a well-tolerated, therapeutic pharmacokinetic profile for interferon therapy in a subject by administration of one or more interferons formulated for short-term delivery to said subject and monitoring said subject for therapeutic and adverse effects; and

b) administering to said subject using at least one internally presented, not externally programmable pump one or more interferons formulated for long-term delivery in which said interferons are released from said pump at a rate that substantially achieves said pharmacokinetic profile during said long-term delivery.

Claim 69 (previously presented): The method of claim 68, further comprising:

c) optionally adjusting the amount of said one or more interferons administered to said subject with an additional long-term formulation of one or more interferons.

Claim 70 (previously presented): The method of claim 68, wherein said rate is a substantially fixed rate.

Claim 71 (previously presented): The method of claim 68, wherein said at least one pump is a plurality of said pumps.

Claim 72 (previously presented): The method of claim 71, wherein each pump releases said one or more interferons at a substantially fixed rate.

Claim 73 (previously presented): The method of claim 68, wherein said pump is an osmotic pump.

Claim 74 (previously presented): A method of individualizing the treatment of an interferon-responsive disorder, comprising:

a) defining a unit dosage of at least one interferon by administering said at least one interferon formulated for short-term delivery to a plurality of subjects to determine the most common optimal dosage; and

b) administering to a subject using one or more internally presented, not externally programmable pumps at least one unit dosage of at least one interferon formulated for long-term delivery and optionally with one or more fractional dosages formulated for long-term delivery

wherein the at least one unit dosage optionally in combination with one or more fractional dosages released from said one or more pumps substantially achieves the unit dosage defined in step a) during said long-term delivery.

Claim 75 (previously presented): The method of claim 74, further comprising:

c) adjusting the one or more unit or fractional dosages administered to said individual subject.

Claim 76 (previously presented): The method of claim 74, wherein said one or more pumps release interferon at a substantially fixed rate.

Claim 77 (previously presented): The method of claim 41, wherein said one or more pumps have fixed delivery rates.

Claim 78 (previously presented): The method of claim 3, wherein said one or more interferons formulated for long-term delivery are selected from the group consisting of natural and recombinant omega interferon and versions thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety is attached.

Claim 79 (previously presented): The method of claim 2, in which there is no overlap in administration of the short-term formulation and the long-term formulation.

Claim 80 (previously presented): The method of claim 68, wherein said long-term delivery is for at least about one month.

Claim 81 (previously presented): The method of claim 68, wherein said long-term delivery is for at least about a quarter year.

Claim 82 (previously presented): The method of claim 22, wherein said at least one interferon formulated for long-term delivery is selected from the group consisting of natural and recombinant omega interferon and versions thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety is attached.

Claim 83 (previously presented): The method of claim 45, wherein said one or more interferons are selected from the group consisting of natural and recombinant omega interferon and versions thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety is attached.

Claim 84 (previously presented): The method of claim 68, wherein said one or more interferons formulated for short-term delivery are not released from the internally presented implantable pump from which said one or more interferons formulated for long-term delivery are released.

Claim 85 (previously presented): The method of claim 71, wherein said at least one interferon formulated for short-term delivery are not released from the internally presented implantable pump from which said one interferon formulated for long-term delivery are released.

Claim 86 (previously presented): A method of treating HCV, comprising: administering to a patient an amount of omega interferon effective to provide therapeutic benefit for at least 3 months, wherein the omega interferon is formulated in an implantable device that is not externally programmable that delivers the omega interferon at a constant rate for said at least 3 months.

Claim 87 (previously presented): A method of treating HCV, comprising:

- a) determining for a patient an amount of omega interferon that has a well-tolerated, therapeutic index for said patient; and
- b) administering to said patient using one or more internally presented, not externally programmable pumps an amount of omega interferon effective to achieve said therapeutic index for a period of 3-12 months.

Claim 88 (previously presented): A method of treating HCV, comprising:

- a) determining for a patient an amount of omega interferon that has a well-tolerated, pharmacokinetic profile for said patient; and

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b) administering to said patient using one or more internally presented, not externally programmable pumps an amount of omega interferon effective to achieve said pharmacokinetic profile for a period of 3-12 months.